Low-Dose Colchicine Effective for Acute Gout

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SAN FRANCISCO — Low-dose colchicine appeared to be as effective as a more conventional dose in treating acute gout flares, but produced far fewer side effects in a randomized, double-blind, placebo-controlled trial in 185 patients.

The results support European League Against Rheumatism 2006 consensus guidelines recommending low doses (0.5 mg t.i.d.) when using colchicine to treat gout flare, a recommendation that was made without the backing of clinical trial data, Dr. Robert A. Terkeltaub said at the annual meeting of the American College of Rheumatology.

The study prerandomized 575 patients to receive high-dose colchicine, low-dose colchicine, or placebo capsules if they called a 24-hour service within 12 hours of the onset of a gout flare. Of the 184 patients who called and received treatment, 52 received high-dose colchicine (1.2 mg, then 0.6 mg hourly for 6 hours, for a total of 4.8 mg); 74 received low-dose colchicine (1.2 mg, then 0.6 mg in 1 hour, for a total of 4.8 mg), and 58 were given placebo (two capsules, then one capsule hourly for 6 hours). One more patient in the placebo group who had no outcomes recorded was excluded from the intent-to-treat analysis of efficacy but included in the safety analysis.

In the only previous placebo-controlled study of colchicine for gout flare, patients on colchicine received a mean total dose of 6.7 mg (higher than the high dose in the current study) and all patients developed diarrhea by the time of clinical response.

In the current study, 33% of patients in the high-dose group and 38% in the low-dose group recorded at least a 50% reduction in pain scores on a seven-point Likert scale within 24 hours of taking the first dose without taking a rescue medication. These rates were significantly higher than the 16% of patients on placebo who achieved this primary outcome. The efficacy between colchicine groups did not differ significantly, said Dr. Terkeltaub, chief of rheumatology in the Veterans Affairs San Diego Healthcare System and professor of medicine at the University of California, San Diego.

The study was funded by Mutual Pharmaceutical Co., a subsidiary of URL Pharma Inc., which manufactures a colchicine tablet. Based on these results, the companies are seeking Food and Drug Administration approval of the medication to treat the pain of gout flares.

Dr. Terkeltaub has been a consultant for AR Scientific, the branded arm of URL Pharma, and for other pharmaceutical companies. One of his coinvestigators is an employee and stockholder in AR Scientific, and other associates have been consultants to that company and to others.

High-dose colchicine produced GI side effects at a significantly higher rate (94%), compared with placebo (28%)—especially diarrhea (77% vs. 14%, respectively).

In the low-dose colchicine group, 45% had GI side effects and 23% developed diarrhea. These rates were not significantly different from those with placebo.

In addition, rates of all adverse events, vomiting, severe adverse events, or severe diarrhea were significantly higher in the high-dose group, compared with the placebo group, but did not differ significantly between patients on low-dose colchicine or placebo.

Patients resorted to rescue medications within 24 hours of the first dose at statistically similar rates in the high-dose group (35%) and placebo group (48%), but the rate of rescue in the low-dose group (28%) was significantly lower than in the placebo group.

While it's good news that a lower dose of colchicine may suffice, it's possible that doses could go lower still, Dr. Terkeltaub said. "Perhaps we need another study" to find the minimum effective dose, he said.

Patients had to have a creatinine clearance rate of at least 60 mL/min to be eligible for the study, and no recent change in the use of serum urate–lowering drugs. A subanalysis found that patients with a higher degree of hyperuricemia (those with serum urate level greater than 10 mg/dL) were less likely to respond to colchicine than patients with lower serum urate levels, he said. ■